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REMDESIVIR AS AN EFFECTIVE DRUG AGAINST COVID-19

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In the past few months, attempts to create an effective drug against the emerging global pandemic,COVID-19, have increased. Drug discovery methods for targeting RNA dependent RNA polymerase (RdRP) of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is being studied globally. The gene encoding this protein, is known to be conserved amongst positive strand RNA viruses. This helps the drugs developed against previously documented RdRP inhibitors to reconfigure a path. Remdesivir, which has been used against EBOLA infections, is one such powerful inhibitor. By using classical molecular dynamics and ensemble docking method, the binding of remdesivir to RdRP of SARS-CoV-2 has been examined. A comparative study of the simulations of RdRP in the apo and remdesivir-bound form revealed blocking of the template entry site in the presence of remdesivir. The conformation changes leading to this event were captured through principal component analysis. The conformational and thermodynamic parameters supported the experimental information available on the involvement of crucial arginine, serine and aspartate residues belonging to the conserved motifs in RdRP functioning. Strong interaction with remdesivir was observed at a catalytic site consisting of SER 759, ASP 760 and ASP 761 (SDD). The considerably strong interactions of Remdesivir and these residues may infer the former's binding similar to the normal nucleotides there by remaining unidentified by the exonuclease activity of RdRP. The ensemble docking of remdesivir too, comprehended the involvement of similar residues in interaction with the inhibitor. In the design of inhibitors, this knowledge on critical interactions between preserved RdRP residues with remdesivir via in silico approaches may be useful.